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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/502,176	02/10/2000	Steven Pirie-Shepherd	05940-0141	4843

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JOHN S. PRATT
KILPATRICK STOCKTON LLP
1100 PEACHTREE
SUITE 2800
ATLANTA, GA 30309

EXAMINER

HARRIS, ALANA M

ART UNIT PAPER NUMBER

1643

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/502,176

Applicant(s)

PIRIE-SHEPHERD ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6-12,15,16,27 and 29-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 27 is/are allowed.
- 6) ☒ Claim(s) 1-4,6, 8-11,15,16,29-33 and 35-38 is/are rejected.
- 7) ☐ Claim(s) 7,12 and 34 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ -Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Response to Arguments

1. Claims 1-4, 6-12, 15, 16, 27 and 29-38 are pending.
Claims 29-38 have been added.
Claims 1-4, 6-12, 15, 16, 27 and 29-38 are examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claim 1-4, 6-12, 15 and 16 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in light of Applicants' arguments.
4. The rejection of claims 1-4, 6-12, 15, 16 and 27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn. In particular, the rejection of claim 4 is withdrawn because it seems that there is only one N-glycosylation site within kringle 1-3 region fragment as indicated in the specification on page 4, line 16-19.

Claim Rejections - 35 USC § 102

5. The rejection of claim 27 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number 2003/0012792 A1 (effective filing date May 22, 1998) is withdrawn in light of the fact SEQ ID NO: 61 is not listed in the priority document, 09/907,402 filed July 17, 2001, now U.S. Patent No. 6,554,947.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-4, 6, 8-11, 15, 16, 29-33 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,837,682 (issued November 17, 1998). U.S. Patent teaches kringles 1-3, a fragment beginning at approximately amino acid 87 of human plasminogen, which can be combined with pharmaceutically acceptable excipients, see column 9, lines 9-13 and 45-49; column 21, lines 5-28; column 22, lines 25-59; column 23, lines 7-21; and column 58, lines 45-53. Kringle 1-3 is an angiostatin fragment, meaning a protein derivative of angiostatin used to inhibit or suppress tumor growth, column 41, lines 19-23 and column 42, lines 47-65.

The patent does not teach a composition comprising a protein consisting of a deglycosylated kringle 1-3 region fragment of a plasminogen protein lacking a bisialylated-biantennary glycan, a N-linked carbohydrate moiety and a carbohydrate chain at amino acid position corresponding to the N-glycosylation site of human plasminogen, further comprising a protein consisting of a naturally glycosylated kringle 1-3 region fragment of a plasminogen protein wherein the amount of the naturally glycosylated kringle 1-3 region fragment in the composition is smaller than the amount of deglycosylated kringle 1-3 region fragment.

However, the patent does teach the expression of angiostatin (kringles 1-4) in *Pichia pastoris* resulting in the expression of a recombinant protein, see column 40, Example 25; see column 51, line 42-column 51, line 18. The *P. pastoris* expressed proteins with N-linked glycosylation, which were digested with endoglycosidase H. The recombinant proteins were also digested with O-glycanase prior to neuraminidase treatment. The expressed protein resulted in two forms: with a N-linked complex chain and without any glycosylation. It would have been *prima facie* obvious at the time of the claimed invention to use the same expression system to manufacture a deglycosylated kringle 1-3 region fragment of a plasminogen protein lacking one or more carbohydrate moieties linked to naturally glycosylated forms of the fragment because it is art known and established in this patent this fragment does have anti-angiogenic activity and angiostatin comprising kringles 1-4 was expressed and exhibited antiangiogenic activity *in vivo* and *in vitro*, see column 42, lines 47-55; column 52, line 19-column 54, line 20. One of ordinary skill in the art would have been motivated to

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express a recombinant antiangiogenic fragment consisting of kringles 1-3 because the art teaches this plasminogen derivative has anti-angiogenic activity *in vivo* and *in vitro*, see column 9, lines 44-49; column 11, lines 4-8; column 42, lines 47-65; and bridging sentence of columns 46 and 47. In addition, the patent also teaches that “[d]ifferent protein fragments of the ... angiostatin molecule can be synthesize for several applications...”, see column 23, lines 55-67.

Moreover, the deglycosylated kringle 1-3 region fragment and the glycosylated form of the fragment are at a ratio of at least 60:40 and 80:20. Since the Patent and Trademark Office does not have the facilities for examining and comparing the disclosed amount produced by the taught recombinant expression method and the established ratio of the claimed invention the burden of proof is upon the Applicants to show an unobvious distinction between the characteristics of the composition in the claimed invention and the composition which can be made based upon the prior art. See *In re Best*, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Allowable Subject Matter

8. Claim 27 is allowed.

9. Claims 7, 12, 27 and 34 are free of the prior art.

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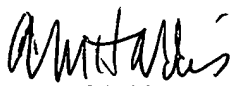
10. Claims 7, 12 and 34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER


Alana M. Harris, Ph.D.
02/18/2005

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12 August 2005